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Lower Plasma Dehydroepiandrosterone Concentration in the Long Term after Severe Accidental Injury

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Dehydroepiandrosterone (DHEA) and its metabolite dehydroepiandrosterone sulfate (DHEAS), which are adrenal gland products like cortisol, show neuroprotective action in animal studies [1] and generally act as noncompetitive antagonists at the $GABA_A$ receptor [1]. A relationship between DHEA(S) concentration, depression, and anxiety disorders including posttraumatic stress disorder (PTSD) has been previously reported [1–5]. The current findings on DHEA(S) concentration in PTSD are however contradictory [2–5]. While the majority of studies have identified a higher DHEA(S) concentration in PTSD subjects than in control subjects, as well as increases in the DHEA(S)-to-cortisol ratio [2, 3], others have reported no group differences [4] or even lower DHEA(S) concentrations in PTSD [5]. The aim of our study was to test chronic/long-term DHEA(S) changes in participants who had developed PTSD after severe accidental injury. In order to disentangle the influence of manifest PTSD symptoms on the plasma DHEA(S) concentrations, we tested only participants with remitted PTSD. In addition, we included a comparison group of survivors of severe accidental injury who had not developed PTSD (trauma controls), and a group of age- and gender-matched non-traumatized healthy subjects (no-trauma controls).

Twenty-nine subjects who experienced severe accidental injury 10 years ago were recruited from our past studies [6–8]. Thirteen participants were diagnosed with PTSD or sub-threshold PTSD [9, 10] according to the DSM-IV in the year following the accident. Fourteen had not developed PTSD during the year after the accident and had no lifetime diagnosis of PTSD. General inclusion criteria were: age between 18 and 70 years, and sufficient proficiency in the German language. Participants were excluded if they had impaired cognitive abilities, current diagnosis of PTSD, current diagnosis of anxiety disorders other than PTSD, psychotic disorders, serious suicidal ideation, psychoactive substance dependence, mental retardation, or a severe major depressive episode. No-trauma subjects were selected from the general population; exclusion criteria were any traumatic events according to the DSM-IV criterion A for PTSD, or any lifetime diagnosis of a mental disorder. Ethical approval was granted by the institutional review board of the canton of Zürich. Written informed consent was obtained from all participants.

Blood samples were taken by venipuncture between 8 and 10 a.m. Cortisol and DHEAS were assessed with competitive electrochemiluminescence immunoassay. DHEA was measured with radioimmunoassay. ANOVA was used for group comparisons. Bonferroni adjustment was used for post hoc comparisons. In all analyses, a two-tailed p value of 0.05 was considered statistically significant. Effect sizes for ANOVAs are reported as eta-squared (η^2) for which values of 0.01, 0.06, and 0.14 are considered to reflect small, medium, and large effects, respectively [11].

Demographic and clinical characteristics are presented in table 1. A significant group effect was found for plasma DHEA concentration ($F_{2, 39} = 3.900$, $p = 0.03$). No significant group effects were obtained in DHEAS concentration ($F_{2, 40} = 0.913$, $p = 0.4$) and DHEA-cortisol ratio ($F_{2, 40} = 2.103$, $p = 0.1$). Post hoc tests only evidenced a significantly lower DHEA concentration in trauma controls compared to the no-trauma group ($p = 0.03$, Bonferroni corrected for multiple comparisons). Adding age as a covariate showed a significant main effect of age, but no significant age-by-group interactions on DHEA, DHEAS, and the DHEA-cortisol ratio, respectively. After controlling for the effect of age, there was a medium effect size of the group factor on DHEA concentration ($F_{2, 38} = 2.623$, $p = 0.09$, $\eta^2 = 0.121$). Gender as an additional between-subject factor in the model did not show any significant main effect.

The unexpected lack of significant differences between the remitted PTSD group and the no-trauma control group could be associated with the remission of the PTSD symptoms, suggesting that there is no difference in DHEA concentrations between PTSD subjects and control subjects after remission. It has been suggested that the increase in DHEA in PTSD is salutary rather than pathophysiologic [3], and there is some indication that effective psychotherapy for PTSD elevates DHEA levels [12]. Thus, the process of remission might have influenced DHEA concentrations in the remitted PTSD group.

The present study has several limitations. Our cross-sectional study design could not explain any causality and intrapersonal chronological hormonal changes, e.g. the decline with aging on DHEA concentration [1]. Blood sampling was done at a single time point; therefore, we could not assess diurnal variation. The sample size is small and the results remain exploratory. Future prospective larger studies are needed to confirm the longitudinal endocrinological influences on accident survivors.

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Table 1. Demographic, clinical, and endocrine characteristics

	Remitted PTSD (n = 13)	Trauma controls (n = 14)	No-trauma controls (n = 16)	Analysis			Effect size
				χ^2 or F	d.f.	p	
1. Sociodemographics and clinical diagnosis							
Female	7 (53.8%)	8 (57.1%)	10 (62.5%)	0.229[a]	2	0.9	
Marital status							
Single	1 (7.7%)	1 (7.1%)	5 (31.3%)				
Married	8 (61.5%)	10 (71.4%)	9 (56.3%)				
Divorced	4 (30.8%)	1 (7.1%)	1 (6.3%)				
Widowed	0	2 (14.3%)	1 (6.3%)				
Employment status							
Paid work	10 (76.9%)	9 (64.3%)	12 (75.0%)				
Unemployed	0	1 (7.1%)	0				
No paid work (homemaker, retired)	3 (23.1%)	4 (28.6%)	4 (25.0%)				
Comorbidity (MINI)							
None	9 (69.2%)	14 (100%)	16 (100%)				
Past major depression	1 (7.7%)	0	0				
Past hypomanic episode	1 (7.7%)	0	0				
Current panic disorder with agoraphobia	1 (7.7%)	0	0				
2. Past treatment for trauma symptoms[b]							
None	9 (69.2%)	14 (100%)	–				
Psychotherapy only	1 (7.7%)	0	–				
Psychotherapy and medication	2 (15.4%)	0	–				
Treatment by family doctor (without medication)	1 (7.7%)	0	–				
3. Treatment status for trauma symptoms at study entry							
None	13 (100%)	14 (100%)	–				
4. Sociodemographics and clinical symptoms							
Age, years	55.5 ± 9.3	58.6 ± 7.1	54.1 ± 10.3	0.980	2, 40	0.4	0.047
Years of education	12.6 ± 4.7	13.9 ± 2.2	15.1 ± 3.9	1.636	2, 40	0.2	0.076
Time since trauma exposure, years[c]	11.4 ± 1.7	9.9 ± 0.3	–	9.612	1, 25	0.005	0.278
Duration of no subjective PTSD symptoms, years	7.5 ± 4.1	–	–				
Current CAPS total score: PTSD	5.3 ± 5.6	2.4 ± 3.9	–	2.414	1, 24	0.1	0.091
STAI: trait anxiety	35.1 ± 5.0	31.7 ± 4.6	35.5 ± 6.6	2.010	2, 40	0.1	0.091
BDI: depression	7.1 ± 3.6	5.4 ± 4.1	5.2 ± 4.5	0.859	2, 40	0.4	0.041
5. Endocrine variables							
Mean time of venipuncture (a.m.)	09:02 (± 29.4 min)	08:58 (± 32.2 min)	08:50 (± 29.2 min)	0.548	2, 38	0.6	0.030
Cortisol, nmol/l	460.4 ± 142.2	453.3 ± 155.2	465.0 ± 137.6	0.025	2, 40	1.0	0.001
DHEA, nmol/l	21.2 ± 8.6	17.3 ± 5.8	27.1 ± 12.6	3.900	2, 39	0.03	0.167
DHEAS, μmol/l	3.7 ± 2.3	2.8 ± 1.4	3.9 ± 2.9	0.913	2, 40	0.4	0.044
DHEA-cortisol ratio	0.054 ± 0.03	0.041 ± 0.02	0.060 ± 0.03	2.103	2, 40	0.1	0.095

Data presented as n (%) or means ± SD. MINI = The Mini International Neuropsychiatric Interview; CAPS = Clinician-Administered PTSD Scale; STAI = State-Trait Anxiety Inventory; BDI = Beck Depression Inventory.

[a] Analyzed using χ^2 test. [b] Psychotherapy: duration is 3 months (n = 1) or 2 years (n = 2). Medication: duration is 1 year (n = 1) or 2 years (n = 1). [c] The trauma survivors (remitted PTSD and trauma control group) came from two cohorts: years 1995–1997 for 6 remitted PTSD participants and 1999–2000 for others. For these 6 remitted PTSD patients, time since trauma exposure was on average 3.2 years longer than for the other remitted PTSD participants and for the trauma controls.

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References

1 Maninger N, Wolkowitz OM, Reus VI, Epel ES, Mellon SH: Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). Front Neuroendocrinol 2009;30:65–91.
2 Gill J, Vythilingam M, Page GG: Low cortisol, high DHEA, and high levels of stimulated TNF-alpha, and IL-6 in women with PTSD. J Trauma Stress 2008;21:530–539.
3 Yehuda R, Brand SR, Golier JA, Yang RK: Clinical correlates of DHEA associated with post-traumatic stress disorder. Acta Psychiatr Scand 2006;114:187–193.
4 Olff M, Guzelcan Y, de Vries GJ, Assies J, Gersons BP: HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. Psychoneuroendocrinology 2006;31:1220–1230.
5 Kanter ED, Wilkinson CW, Radant AD, Petrie EC, Dobie DJ, McFall ME, Peskind ER, Raskind MA: Glucocorticoid feedback sensitivity and adrenocortical responsiveness in posttraumatic stress disorder. Biol Psychiatry 2001;50:238–245.
6 Hepp U, Moergeli H, Buchi S, Bruchhaus-Steinert H, Kraemer B, Sensky T, Schnyder U: Post-traumatic stress disorder in serious accidental injury: 3-year follow-up study. Br J Psychiatry 2008;192:376–383.
7 Schnyder U, Moergeli H, Klaghofer R, Buddeberg C: Incidence and prediction of posttraumatic stress disorder symptoms in severely injured accident victims. Am J Psychiatry 2001;158:594–599.
8 Schnyder U, Wittmann L, Friedrich-Perez J, Hepp U, Moergeli H: Posttraumatic stress disorder following accidental injury: Rule or exception in Switzerland? Psychother Psychosom 2008;77:111–118.
9 Blanchard EB, Hickling EJ, Taylor AE, Loos W: Psychiatric morbidity associated with motor vehicle accidents. J Nerv Ment Dis 1995;183:495–504.
10 Stein MB, Walker JR, Hazen AL, Forde DR: Full and partial posttraumatic stress disorder: findings from a community survey. Am J Psychiatry 1997;154:1114–1119.
11 Cohen J: Eta-squared and partial eta-squared in communication science. Human Comm Res 1973;28:473–490.
12 Olff M, de Vries GJ, Guzelcan Y, Assies J, Gersons BP: Changes in cortisol and DHEA plasma levels after psychotherapy for PTSD. Psychoneuroendocrinology 2007;32:619–626.

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